FIGURE 1

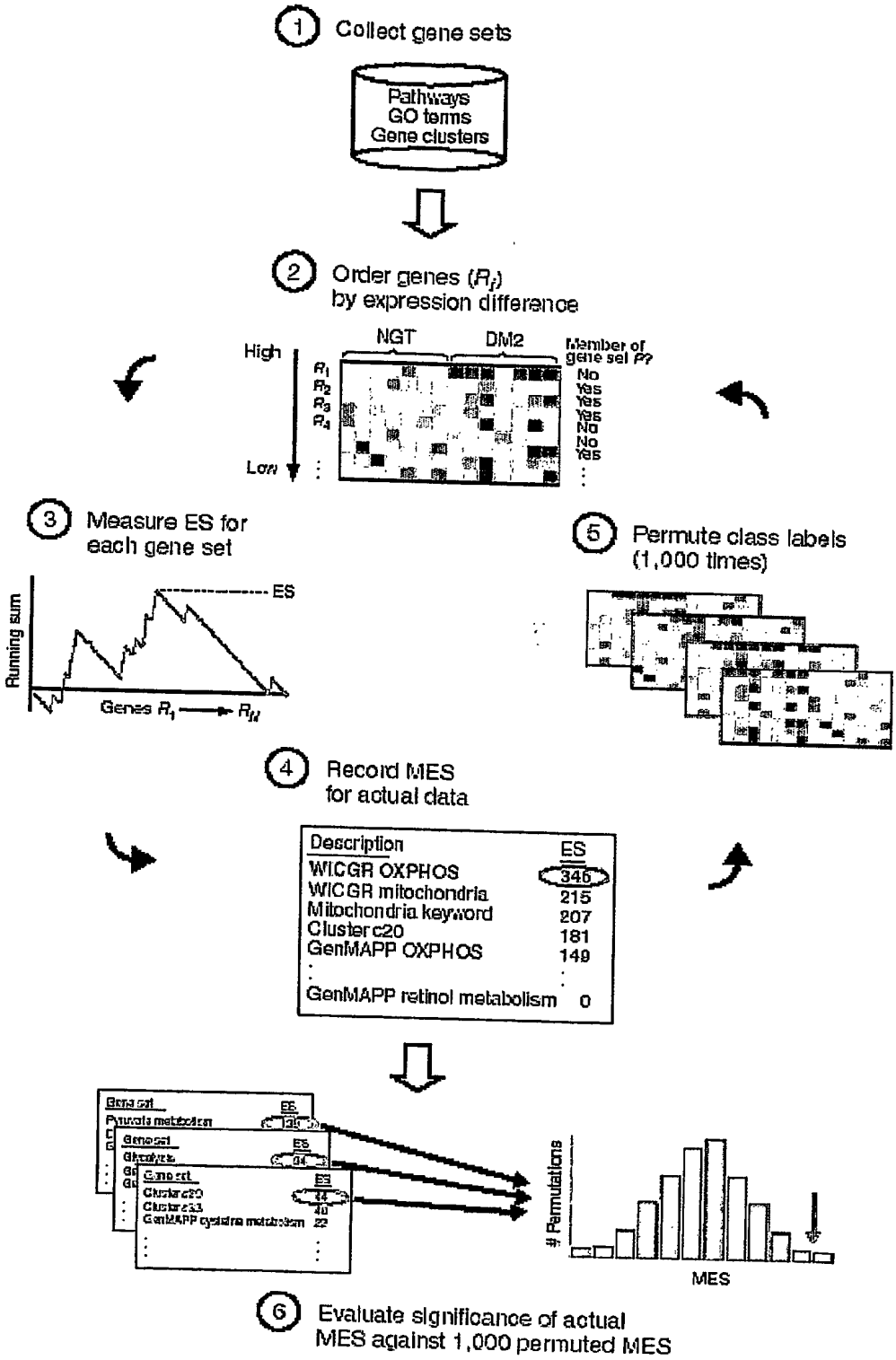

1 Collect gene sets
Pathways
GO terms
Gene clusters
2 Order genes (R_j) by expression difference
NGT
DM2
Member of gene set P?
High
Low
R_1
R_2
R_3
R_4
No
Yes
Yes
Yes
No
No
Yes
3 Measure ES for each gene set
ES
Running sum
Genes R_1 → R_N
5 Permute class labels (1,000 times)
4 Record MES for actual data
Description ES
WICGR OXPHOS 346
WICGR mitochondria 215
Mitochondria keyword 207
Cluster c20 181
GenMAPP OXPHOS 149
GenMAPP retinol metabolism 0
Permutations
MES
6 Evaluate significance of actual MES against 1,000 permuted MES

FIGURE 2

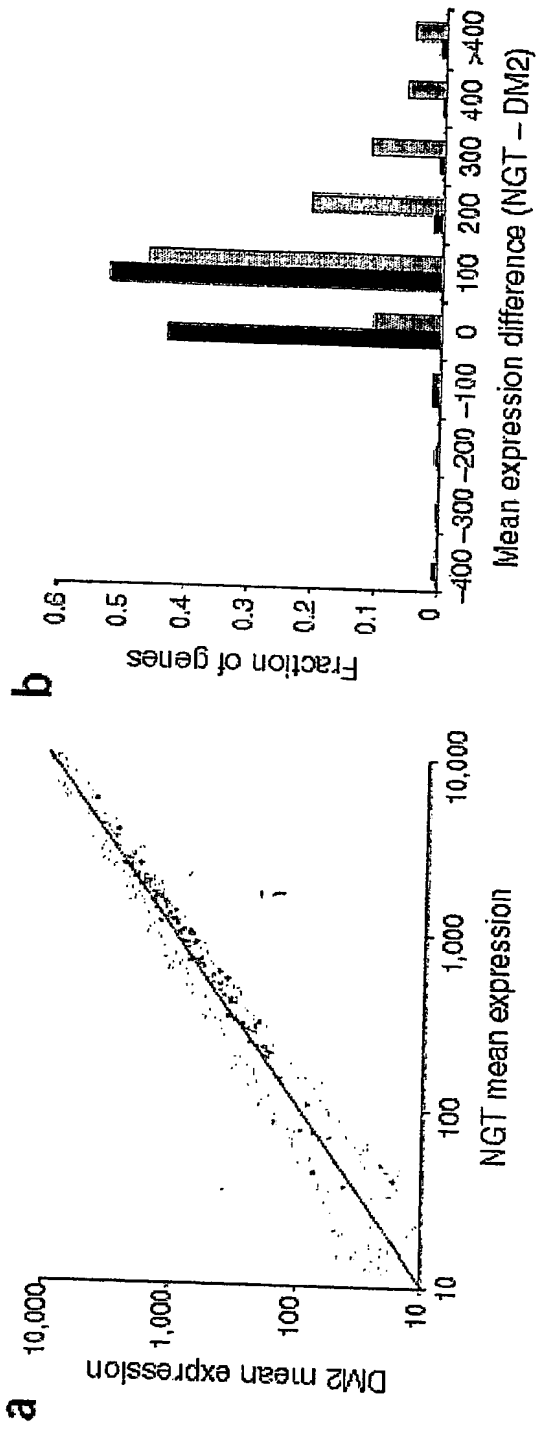

a
DM2 mean expression
10,000
1,000
100
10
10
100
1,000
10,000
NGT mean expression
b
Fraction of genes
0.6
0.5
0.4
0.3
0.2
0.1
0
−400 −300 −200 −100 0 100 200 300 400 >400
Mean expression difference (NGT – DM2)

FIGURE 3

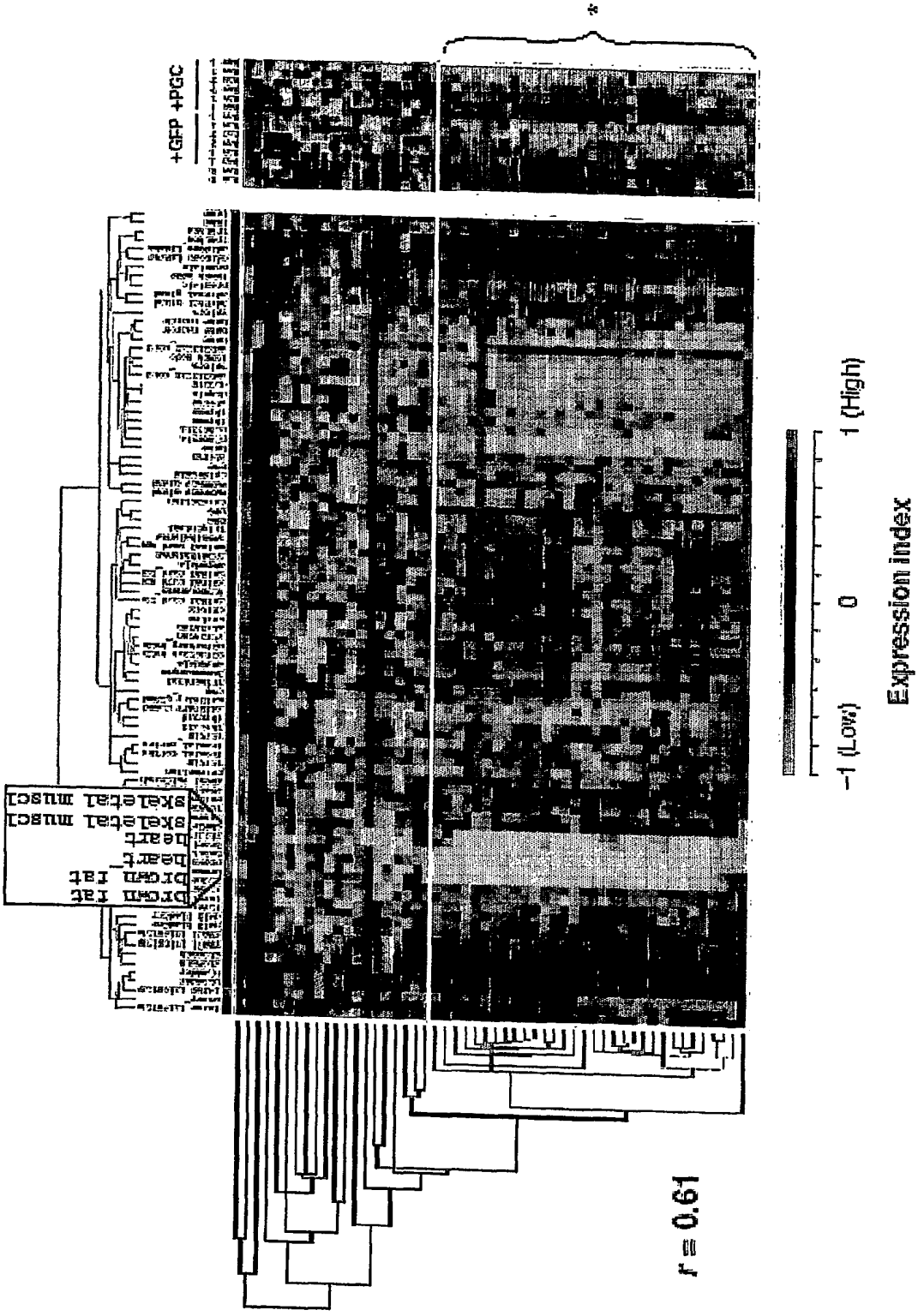

+GFP +PGC
Expression index
1 (High)
0
-1 (Low)
r = 0.61
skeletal musc
skeletal musc
heart
heart
brown fat
brown fat

FIGURE 4

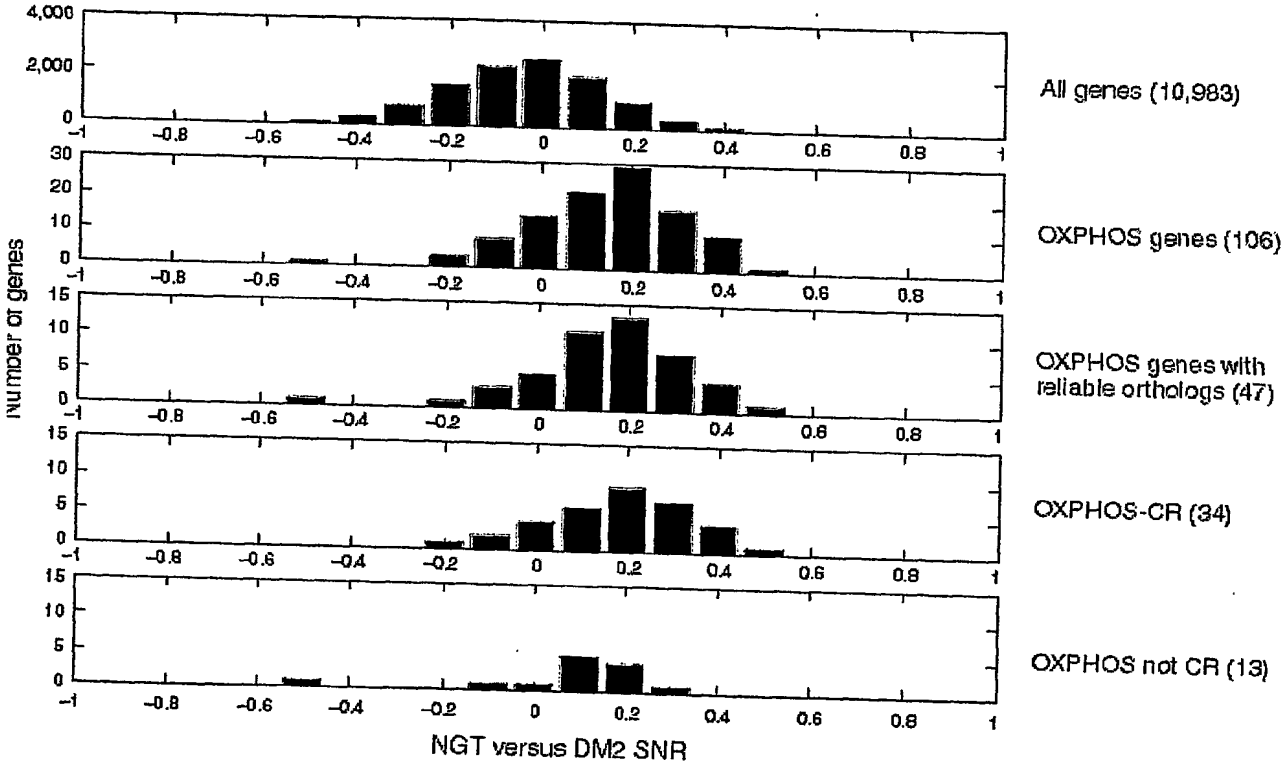

Number of genes
NGT versus DM2 SNR
All genes (10,983)
OXPHOS genes (106)
OXPHOS genes with reliable orthologs (47)
OXPHOS-CR (34)
OXPHOS not CR (13)

FIGURE 5

	Predictor(s)	R^2_{adj}	*P* value
	Diabetes status	0.28	0.0006
1	OXPHOS-CR	0.22	0.0012
1	Diabetes status, OXPHOS-CR	0.33	0.0004
2	*UQCRB*	0.31	<0.0001
2	Diabetes status, *UQCRB*	0.38	0.0001

[1] Addition of OXPHOS-CR improves the model with $P = 0.05$.

[2] Addition of *UQCRB* improves the model with $P = 0.03$.

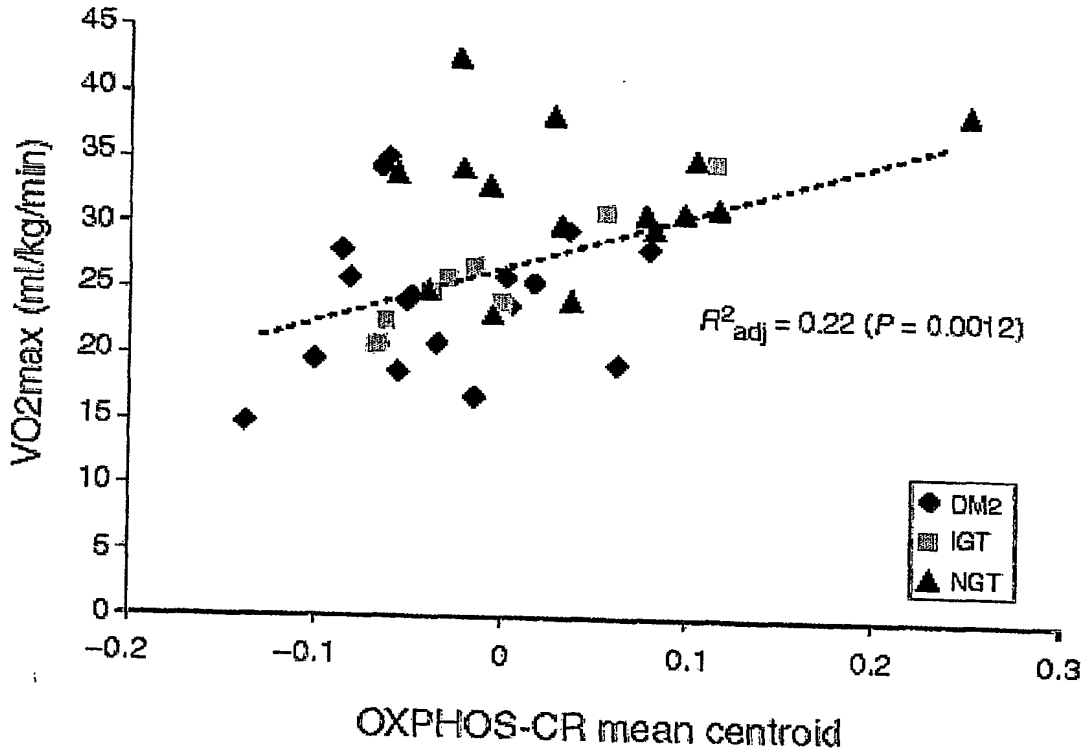


FIGURE 6

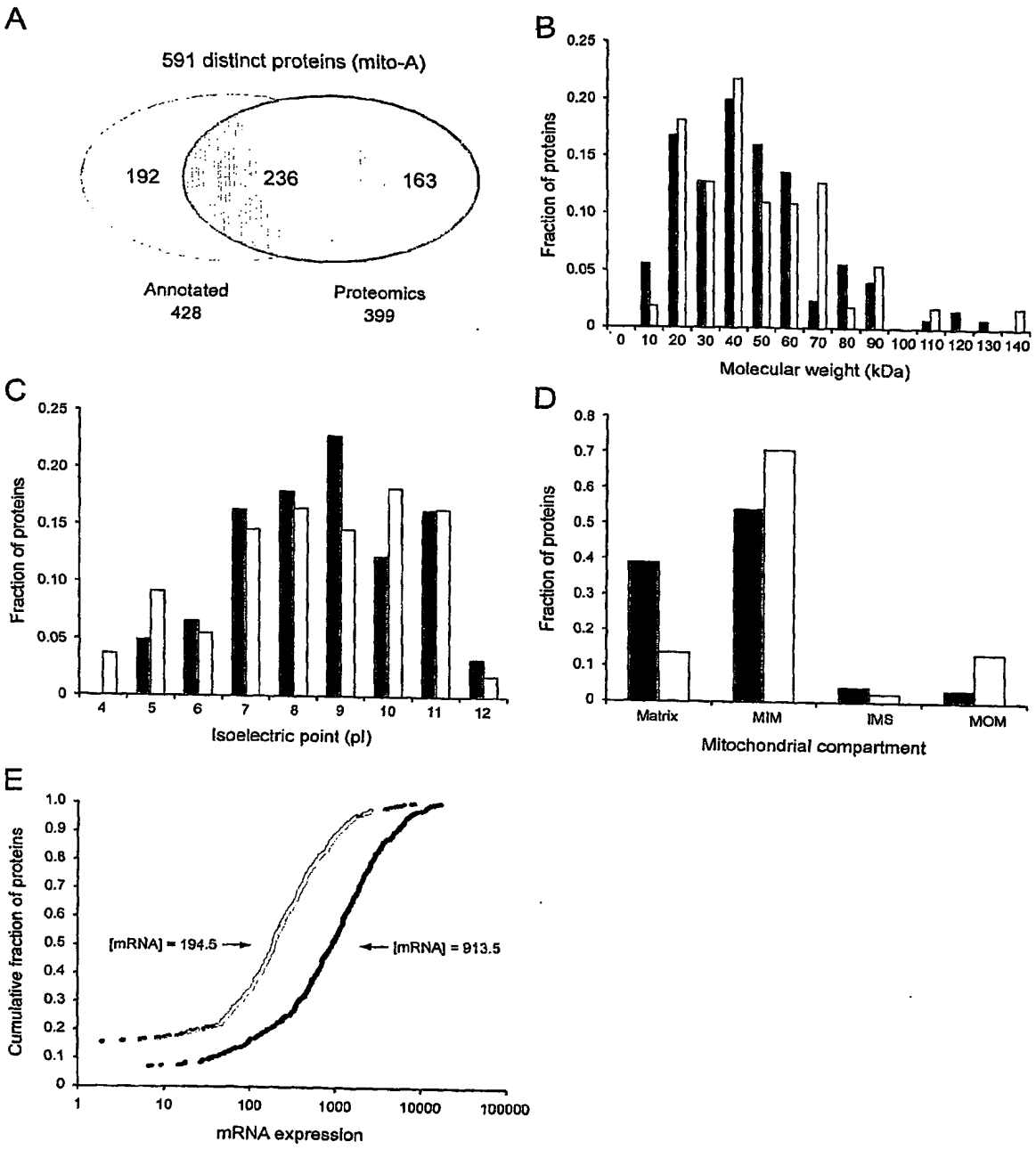

A
591 distinct proteins (mito-A)
192
236
163
Annotated
428
Proteomics
399
B
Fraction of proteins
0.25
0.20
0.15
0.10
0.05
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140
Molecular weight (kDa)
C
Fraction of proteins
0.25
0.20
0.15
0.10
0.05
0
4 5 6 7 8 9 10 11 12
Isoelectric point (pI)
D
Fraction of proteins
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Matrix
MIM
IMS
MOM
Mitochondrial compartment
E
Cumulative fraction of proteins
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
[mRNA] = 194.5
[mRNA] = 913.5
1
10
100
1000
10000
100000
mRNA expression

FIGURE 7

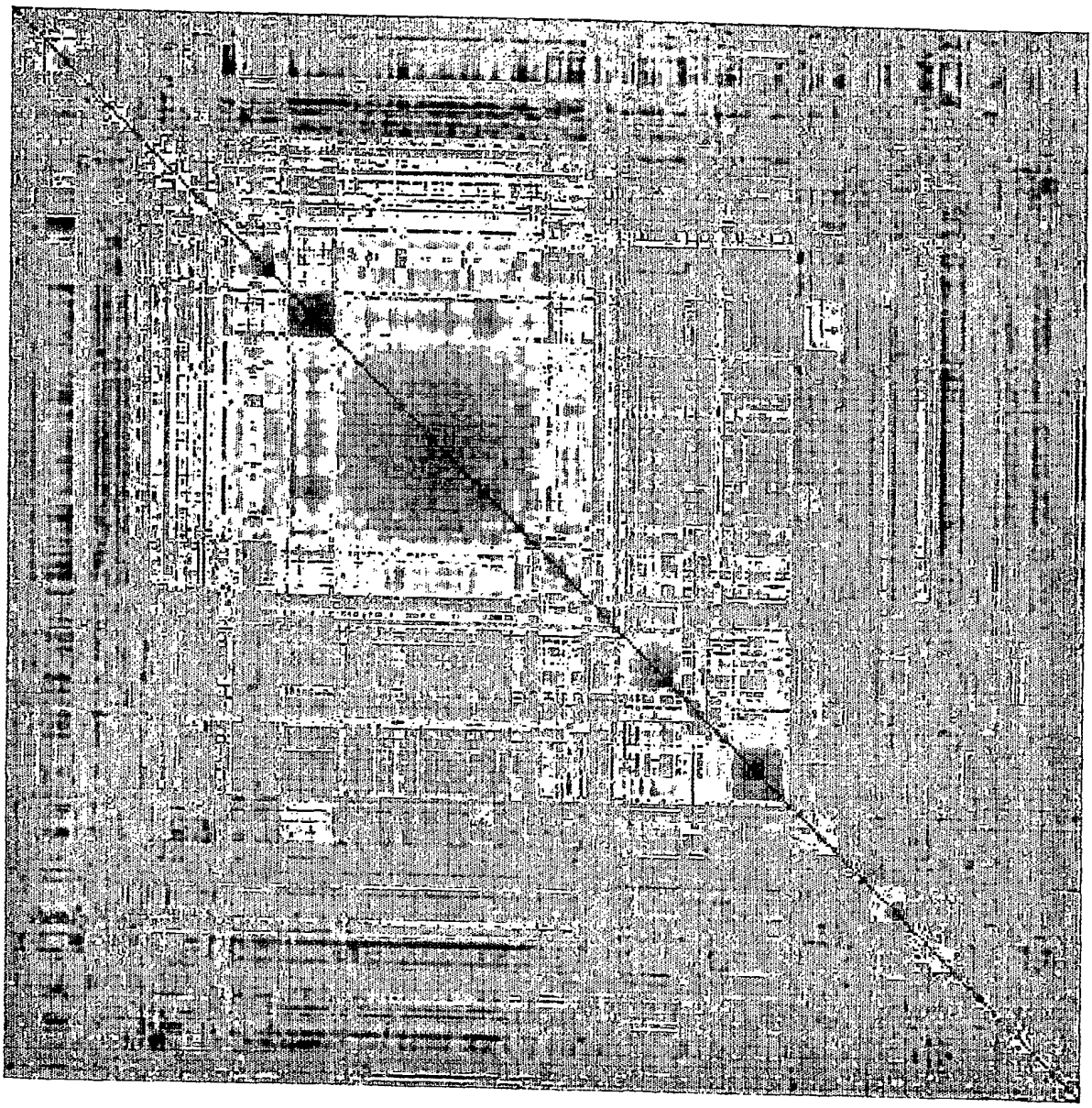


FIGURE 8

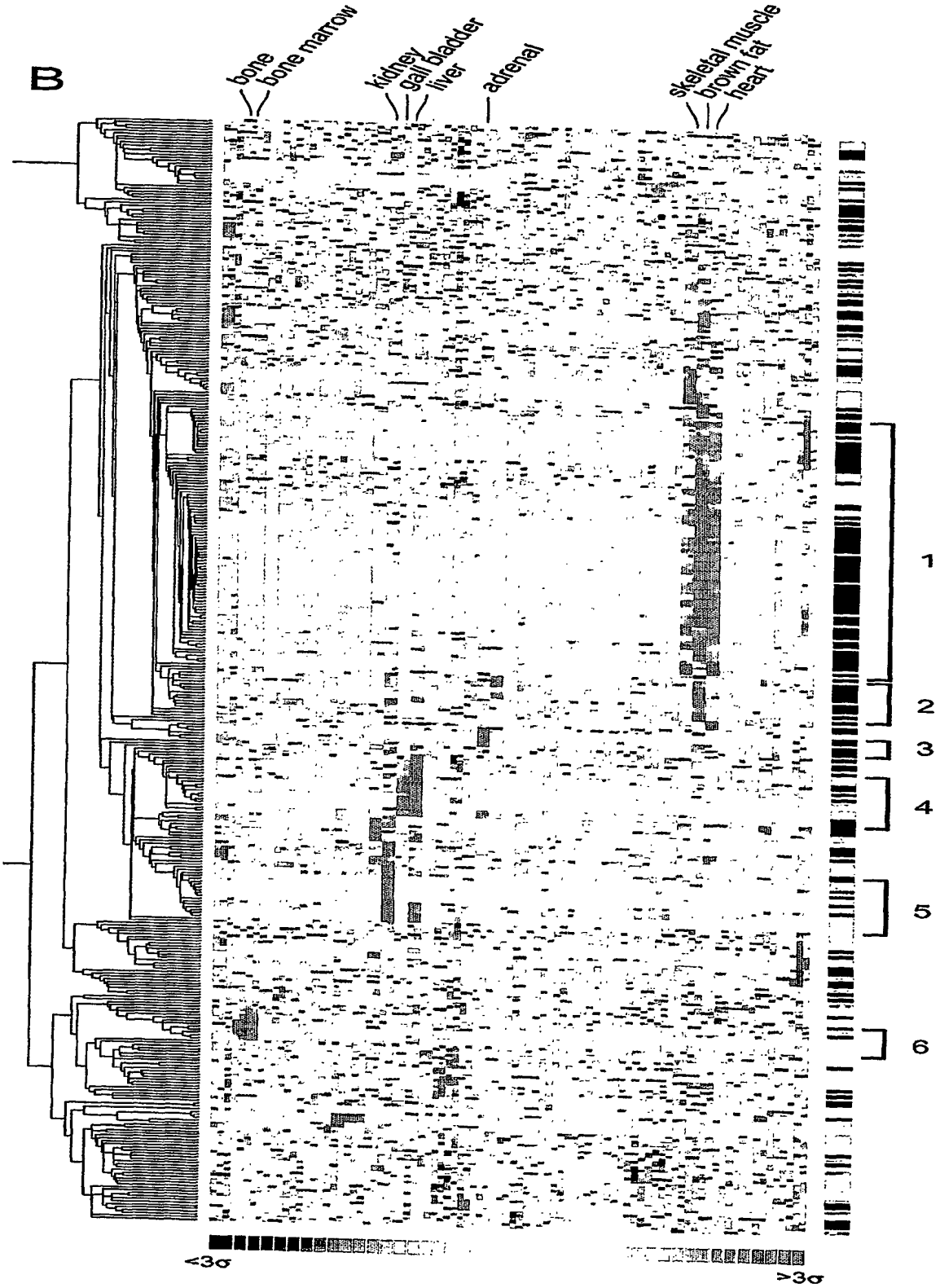

B
bone
bone marrow
kidney
gall bladder
liver
adrenal
skeletal muscle
brown fat
heart
1
2
3
4
5
6
<3σ
>3σ

FIGURE 9

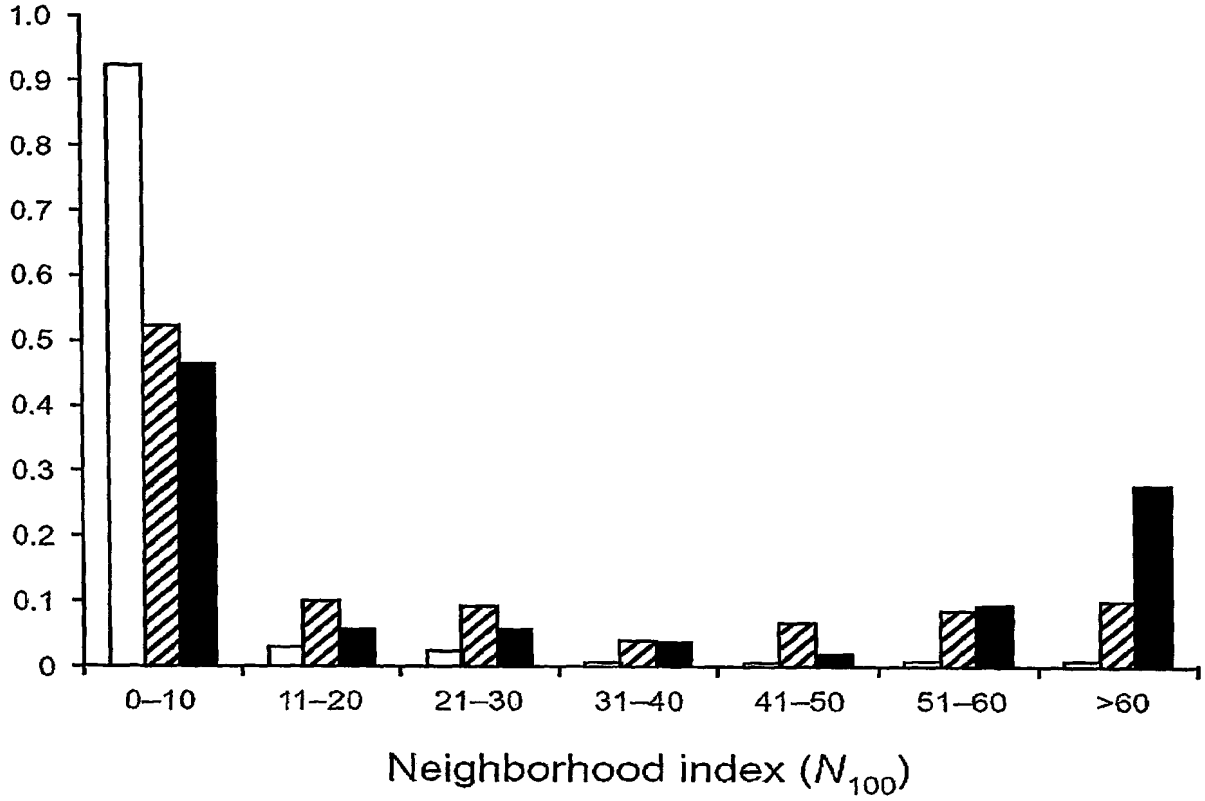

1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0–10
11–20
21–30
31–40
41–50
51–60
>60
Neighborhood index (N_{100})

FIGURE 10

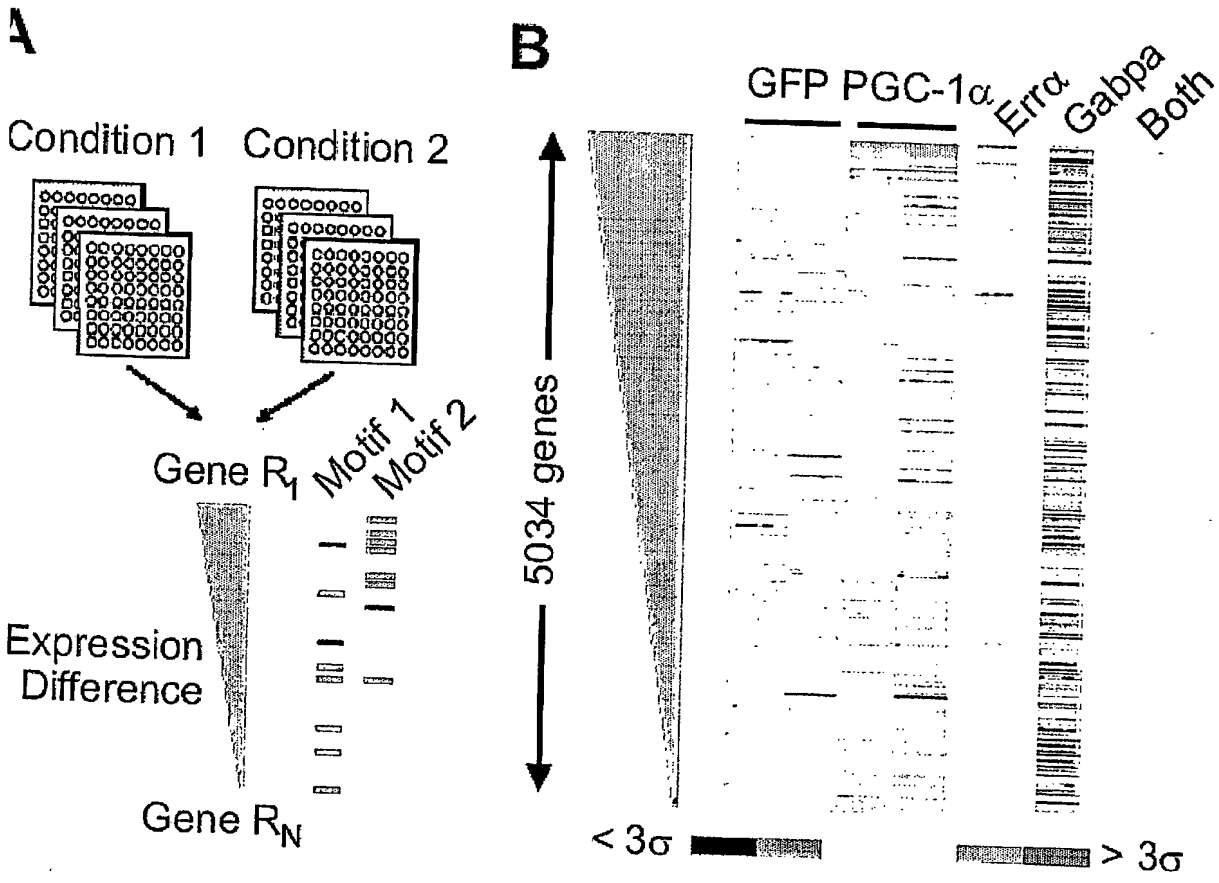

A
Condition 1
Condition 2
Gene R_1
Motif 1
Motif 2
Expression Difference
Gene R_N
B
GFP
PGC-1α
Errα
Gabpa
Both
5034 genes
< 3σ
> 3σ

FIGURE 11

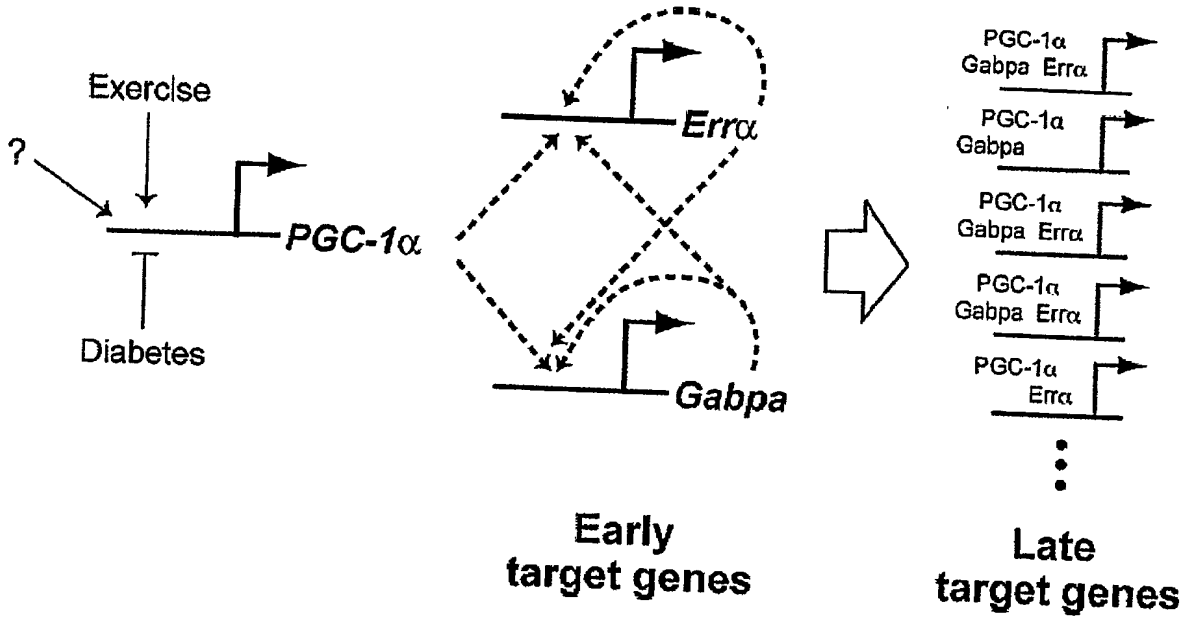
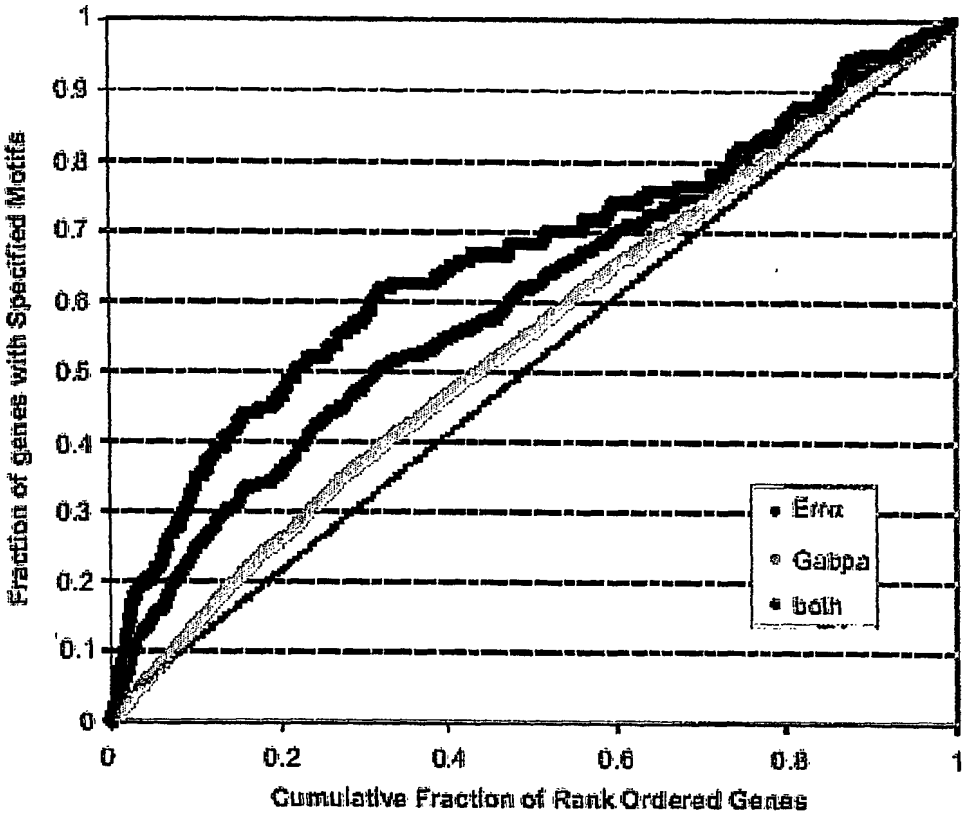

Exercise
?
PGC-1α
Diabetes
Errα
Gabpa
Early target genes
PGC-1α Gabpa Errα
PGC-1α Gabpa
PGC-1α Gabpa Errα
PGC-1α Gabpa Errα
PGC-1α Errα
Late target genes

FIGURE 12


Fraction of genes with Specified Motifs
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.2
0.4
0.6
0.8
1
Cumulative Fraction of Rank Ordered Genes
Erra
Gabpa
both